Complete Summary

GUIDELINE TITLE

Practice parameter: antiepileptic drug prophylaxis in severe traumatic brain injury: report of the Quality Standards Subcommittee of the American Academy of Neurology.

BIBLIOGRAPHIC SOURCE(S)

Chang BS, Lowenstein DH. Practice parameter: antiepileptic drug prophylaxis in severe traumatic brain injury: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2003 Jan 14;60(1):10-6. [32 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Traumatic brain injury
- Seizures

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Prevention

CLINICAL SPECIALTY

Emergency Medicine
Neurology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations for the prophylactic use of antiepileptic drugs (AEDs) in patients with severe traumatic brain injury (TBI)

TARGET POPULATION

Adult patients with severe traumatic brain injury (TBI)

INTERVENTIONS AND PRACTICES CONSIDERED

Antiepileptic drugs (phenytoin, carbamazepine, valproate) given prophylactically

MAJOR OUTCOMES CONSIDERED

Rates of early and late post-traumatic seizure in patients given antiepileptic drug (AED) prophylaxis versus controls

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Guideline developers searched Medline, Science Citation Index, the Cochrane Database, and Current Contents by combining the search terms "head trauma," "head injury," or "brain injury" with the terms "seizure" or "epilepsy" (including all related terms and subheadings). The abstracts of the identified references were reviewed to find those that reported on the clinical use of post-traumatic seizure prophylaxis in humans. Fifty-four length articles were initially examined, as well as 12 others identified by reviewing both the reference lists of the initial articles found and those of relevant review articles, meta-analyses, and book chapters

Inclusion/Exclusion Criteria

Guideline developers selected studies that met the following eligibility criteria:

1. Prospective design

2. Random or nonrandom assignment of traumatic brain injury (TBI) patients to a group receiving antiepileptic drug (AED) prophylaxis or a control group (placebo use not required)
3. Reporting of post-traumatic seizure rates in the treated and control groups
4. Publication in a peer-reviewed journal in any language (abstracts or publications reporting preliminary data only were excluded). In cases in which multiple publications reported ongoing results from the same study, guideline developers used the publication with the most complete data and longest duration of follow-up.

All studies meeting the criteria enrolled only patients considered by the studies´ authors to have severe traumatic brain injury (typically with loss of consciousness or amnesia for more than 12 or 24 hours, intracranial hematoma, depressed skull fracture, and/or brain contusion present on computed tomography scan). This included patients with both penetrating and closed types of head injury. Also, all studies distinguished between early post-traumatic seizures (those occurring within and inclusive of 7 days of injury) and late seizures (those occurring thereafter).

NUMBER OF SOURCE DOCUMENTS

Fifty-four full-length articles were initially examined, as well as 12 others identified by reviewing the reference lists of the initial articles found and those of relevant review articles, meta-analyses, and book chapters.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Classification of Evidence

Class I: Evidence provided by a randomized, controlled clinical trial (RCT) with masked outcome assessment in a representative population. The following are required: a) primary outcomes are clearly defined; b) exclusion and inclusion criteria are clearly stated; c) there is adequate accounting of dropouts and crossovers with numbers sufficiently low to have minimal potential for bias; and d) relevant baseline characteristics are substantially equivalent among treatment groups. For the purposes of this parameter, a loss-to-follow-up rate of <10% was required to meet criterion c.

Class II: Evidence provided by a prospective matched group cohort study in a representative population with masked outcome assessment that meets a through d above or an RCT that lacks one criterion a through d.

Class III: All other controlled trials (including well-defined natural history controls or patients serving as their own controls) in a representative population where outcome assessment is independent of patient treatment.

Class IV: Evidence from studies not assessing outcomes independent of treatment, uncontrolled studies, case series, case reports, or expert opinion.

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

For each study, guideline developers extracted details on methodology and findings to the extent available in the publication. They then graded the quality of evidence. The grading of each study was performed by consensus between the authors. For each study, guideline developers compared the proportion of patients with early or late post-traumatic seizures in the treated group to that in the control group by calculating the relative risk (RR) and a 95% confidence interval. When the appropriate data were available in the publication, the developers calculated these relative risks based on intention to treat, analyzing all patients assigned to each treatment group as if they actually received that treatment. Comparisons between treated and control groups were performed using Fisher's exact test. When necessary, they pooled data from multiple studies to obtain more precise relative risks, using general variance-based meta-analytic techniques. Although there are limitations to the conclusions that can be drawn from combined evidence, they began by pooling class I studies first to minimize the risk of bias in pooled comparisons.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendations

Level A: Established as effective, ineffective, or harmful for the given condition in the specified population. Usually, an "A" recommendation requires that the pooled result from two or more distinct class I studies demonstrates a consistent, significant, and important effect.

Level B: Probably effective, ineffective, or harmful for the given condition in the specified population. Usually, a "B" recommendation requires that a single class I study demonstrates a significant and important effect or the pooled result from two or more distinct class II studies demonstrates a consistent, significant, and important effect.

Level C: Possibly effective, ineffective, or harmful for the given condition in the specified population. Usually, a "C" recommendation requires that a single class II study demonstrates a significant and important effect or the pooled result of two or more distinct class III studies demonstrates a consistent, significant, and important effect.

Level U: Data are inadequate or conflicting. Given current knowledge, treatment is unproven and an evidence-based recommendation cannot be made.

Note: Stronger recommendations were made when evidence showing a consistent and significant effect was derived from studies with lesser risks of bias. When combined evidence was used, the subcommittee downgraded the strength of the recommendation to that appropriate for the lowest class of evidence (that with the highest risk of bias) included among the pooled studies.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Draft guidelines were reviewed for accuracy, quality, and thoroughness by the American Academy of Neurology (AAN) members, topic experts, and pertinent physician organizations.

Final guidelines were approved by the Quality Standards Subcommittee on March 2, 2002, the Practice Committee on August 13, 2002, and the American Academy of Neurology Board of Directors on October 19, 2002. They were published in Neurology 2003;60:10-16.

The guideline developers compared their recommendations with those from three other national specialty organizations and found them to be generally consistent.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the strength of the recommendations (Level A, B, C, U) and classification of evidence (Class I-IV) are provided at the end of the "Major Recommendations" field.

Practice Recommendations

For adult patients with severe traumatic brain injury (TBI) (typically with prolonged loss of consciousness or amnesia, intracranial hematoma or brain contusion on computed tomography [CT] scan, and/or depressed skull fracture):

- Prophylactic treatment with phenytoin, beginning with an intravenous (IV) loading dose, should be initiated as soon as possible after injury to decrease the risk of post-traumatic seizures occurring within the first 7 days (Level A).

- Prophylactic treatment with phenytoin, carbamazepine, or valproate should not routinely be used beyond the first 7 days after injury to decrease the risk of post-traumatic seizures occurring beyond that time (Level B).

These recommendations are generally consistent with those from other national specialty organizations, as well as with the findings on post-traumatic seizures from a recent meta-analysis (as of 2001) of antiepileptic drug (AED) prophylactic effect in a variety of epileptogenic conditions.

Definitions:

Strength of Recommendations

Level A: Established as effective, ineffective, or harmful for the given condition in the specified population. Usually, an "A" recommendation requires that the pooled result from two or more distinct class I studies demonstrates a consistent, significant, and important effect.

Level B: Probably effective, ineffective, or harmful for the given condition in the specified population. Usually, a "B" recommendation requires that a single class I study demonstrates a significant and important effect or the pooled result from two or more distinct class II studies demonstrates a consistent, significant, and important effect.

Level C: Possibly effective, ineffective, or harmful for the given condition in the specified population. Usually, a "C" recommendation requires that a single class II study demonstrates a significant and important effect or the pooled result of two or more distinct class III studies demonstrates a consistent, significant, and important effect.

Level U: Data are inadequate or conflicting. Given current knowledge, treatment is unproven and an evidence-based recommendation cannot be made.

Classification of Evidence

Class I: Evidence provided by a randomized, controlled clinical trial (RCT) with masked outcome assessment in a representative population. The following are required: a) primary outcomes are clearly defined; b) exclusion and inclusion criteria are clearly stated; c) there is adequate accounting of dropouts and crossovers with numbers sufficiently low to have minimal potential for bias; and d) relevant baseline characteristics are substantially equivalent among treatment groups. For the purposes of this parameter, a loss-to-follow-up rate of <10% was required to meet criterion c.

Class II: Evidence provided by a prospective matched group cohort study in a representative population with masked outcome assessment that meets a through d above or an RCT that lacks one criterion a through d.

Class III: All other controlled trials (including well-defined natural history controls or patients serving as their own controls) in a representative population where outcome assessment is independent of patient treatment.

Class IV: Evidence from studies not assessing outcomes independent of treatment, uncontrolled studies, case series, case reports, or expert opinion.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- These guidelines may assist physicians in making appropriate clinical decisions regarding the prophylactic use of antiepileptic drugs (AEDs) in patients with severe traumatic brain injury (TBI).
- For adult patients with severe traumatic brain injury, prophylaxis with phenytoin is effective in decreasing the risk of early post-traumatic seizures. Pooled studies demonstrated a significantly lower risk of early post-traumatic seizures (those occurring within 7 days after injury) in patients given phenytoin prophylaxis compared to controls (relative risk 0.37, 95% confidence interval 0.18 to 0.74).

POTENTIAL HARMS

Adverse Effects of Antiepileptic Drugs

Rash was the most commonly reported idiosyncratic reaction to phenytoin, and lethargy and fatigue were the most common side effects reported for valproate in the studies reviewed for this guideline.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The American Academy of Neurology recognize that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Jan 14

GUIDELINE DEVELOPER(S)

American Academy of Neurology - Medical Specialty Society

SOURCE(S) OF FUNDING

American Academy of Neurology (AAN)

GUIDELINE COMMITTEE

Quality Standards Subcommittee of the American Academy of Neurology

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

AAN Quality Standards Subcommittee Members: Gary Franklin, MD, MPH (Co-Chair); Catherine Zahn, MD (Co-Chair); Milton Alter, MD, PhD; Stephen Ashwal, MD; Richard M. Dubinsky, MD; Jacqueline French, MD; Gary Friday, MD; Michael Glantz, MD (Facilitator); Gary Gronseth, MD; Deborah Hirtz, MD; Robert G. Miller, MD; David J. Thurman, MD, PhD; and William Weiner, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the AAN Web site.

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 1080 Montreal Avenue, St. Paul, MN 55116.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology.

Electronic copies: Available from the American Academy of Neurology Web site.

PATIENT RESOURCES

None available

NGC STATUS

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